# ACE BRIEF FOR NEW AND EMERGING HEALTH TECHNOLOGIES

# Artificial intelligence-enabled electrocardiogram (AI-ECG) to detect reduced left ventricular ejection fraction

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# Contents

## Summary of Key Points

- Heart failure (HF) affects 4.5% of Singapore's population with poor prognosis yet is often diagnosed late due to limited access to left ventricular ejection fraction (LVEF) assessment via echocardiography, particularly in primary care settings, which requires technical expertise and substantial operating costs.
- Artificial intelligence-enhanced electrocardiography (AI-ECG) tools can detect LVEF levels using electrocardiogram (ECG) signals, enabling early identification of HF by detecting low LVEF. At the time of review, AI-ECG tools approved by the US Food and Drug Administration (FDA) for classifying LVEF ≤40% include Anumana ECG-AI LEF, Tempus ECG-Low EF and Bunkerhill ECG-EF, which all analyse 12-lead ECG inputs, as well as Eko ELEFT that analyses single-lead ECG inputs obtained from a digital stethoscope.
- The key evidence base comprises seven studies for the Eko and Anumana AI-ECG tools, including two randomised controlled trials (RCTs), four prospective observational studies and one cost-effectiveness study. No published literature was identified for the Tempus ECG-Low EF and Bunkerhill ECG-EF tools.
- Overall, Eko and Anumana AI-ECG tools were found to be safe with moderate accuracy in detecting LVEF ≤40%.
    - No serious adverse events (AE) were reported with similar composite AE observed between AI-ECG and usual care arms (odds ratio [OR], 1.00; p=0.975).
    - Both tools demonstrated moderate to good accuracy in distinguishing LVEF ≤40% when compared to echocardiography (overall sensitivity, 76.5% to 100%; specificity, 78.3% to 97%; negative predictive value, 98% to 100%). Only positive predictive value (PPV) was low ( 16.4% to 43.3%).
    - Anumana appeared to perform better than Eko in terms of specificity (97% *vs.* 78.3% to 81.8%) and PPV (43.3% *vs.* 16.4% to 35.1%).
- However, evidence for clinical utility remains limited.
    - Compared to usual care, Anumana showed minimal impact in detecting low LVEF (0.9% vs. 0.6%, p=0.057) and did not significantly alter guideline-directed medical therapy.
    - Compared to usual care, use of the Eko and Anumana tools showed similar composite cardiovascular events (OR, 1.10; p=0.621) and cardiovascular-related mortality (HR, 1.75; p=0.442) in pregnant and postpartum women.
    - Some evidence suggests that Eko ELEFT may have prognostic value, with predicted low LVEF showing significant associations with major adverse cardiovascular event (hazard ratio [HR], 1.93; p=0.0001) and all-cause mortality (HR, 1.56; p=0.024) in multivariate analysis, suggesting its potential as an independent risk assessment tool.
- These findings require cautious interpretation due to non-systematic echocardiographic assessment in control groups, potential inter-operator variability in LVEF assessment, unclear impact on long-term patient outcomes, and limited generalisability of the findings to the local population.

- One economic evaluation showed that Anumana was cost-effective with an incremental cost-effectiveness ratio (ICER) of US$27,858 per quality-adjusted life year (QALY) compared to usual care, particularly in the outpatient setting (ICER: US$1,651 per QALY).
- No local cost information was identified for AI-ECG tools although a cost of US$100 per analysis was assumed in the cost-effectiveness study.
- Key implementation challenges include securing clinician buy-in and trust, establishing robust clinical governance and cybersecurity frameworks, ensuring seamless workflow integration, and managing potential increases in echocardiography referral volumes without overwhelming existing healthcare resources.
- Three ongoing studies are evaluating AI-ECG tools with estimated completion dates between 2024 and 2026. Two studies are examining Eko ELEFT's clinical and system-level outcomes, while a RCT is investigating the impact of Tempus ECG-Low EF on low LVEF detection and patient outcomes. However, the RCT has not yet begun recruiting, creating uncertainty around its completion timeline.
- Aside from the FDA-cleared AI-ECG tools, several other commercial software solutions to detect for low LVEF have been approved in Europe or South Korea. Some of these tools can detect multiple structural heart diseases, including low LVEF.
- Local clinicians across public healthcare clusters identified AI-ECG tools as valuable for early detection and triage of LVEF, particularly for upstream screening in high-risk patients and optimising echocardiography resource allocation, with primary care and emergency departments viewed as promising initial deployment sites.

## I. Background

Heart failure (HF) is a clinical syndrome arising from structural or functional impairment of the ventricles, leading to symptomatic left ventricular systolic dysfunction (LVSD).[1] Owing to insufficient cardiac output and failure to meet the metabolic demands of the body, the symptoms of HF include shortness of breath, fatigue, oedema and tachycardia.[2] However, patients with asymptomatic LVSD may experience HF without any clinical signs.

Following diagnosis, HF is further classified based on left ventricular ejection fraction (LVEF)as HF with reduced ejection fraction (HFrEF; LVEF ≤40%), HF with mildly reduced ejection fraction (LVEF, 41% to 49%), and HF with preserved ejection fraction (LVEF ≥50%).[1] Among these subtypes, HFrEF represents the most severe form of HF and is associated with the highest mortality rate.[1]

Globally, HF presents a challenge to healthcare systems.[2] In Singapore, HF affects 4.5% of the total population compared to 1% to 2% in the United States and Europe.[3] The condition carries a poor prognosis, with a two-year mortality rate of 37.1% for local patients with HFrEF.[4] The disease burden is expected to worsen as HF prevalence increases with age, coinciding with Singapore's ageing population.[1]

A key challenge is that HF is often a late diagnosis, occurring once a patient presents to the hospital. This results in missed opportunities for early intervention and prevention of disease

progression.[5] Current LVEF assessment relies on echocardiography, but the technical expertise required to conduct echocardiography and accurately measure LVEF, combined with substantial operational costs, limits its widespread deployment in Singapore's healthcare system (Personal communication, Senior Consultant, from Changi General Hospital, 28 October 2025). This diagnostic bottleneck is also evident internationally. In the UK 80% of HF cases are diagnosed in hospital settings, despite 40% of these patients having previously reported HF symptoms to their primary care provider, where an earlier assessment could have been performed.[6] Furthermore, identifying patients with asymptomatic LVSD remains challenging.

Together, these factors highlight an unmet clinical need for earlier HF diagnosis, particularly in primary care settings where echocardiography access is limited, to allow timely interventions that could prevent disease progression.

## II. Technology and Regulatory Status

Artificial intelligence-enhanced electrocardiography (AI-ECG) uses advanced deep learning methods, particularly convolutional neural networks, to analyse standard electrocardiogram (ECG) signals.[7] These AI models learn to identify ECG signatures and subtle patterns that are often imperceptible to the human eye, effectively transforming ECG into a non-invasive digital biomarker for various cardiovascular conditions.[7] Among its clinical applications, AI-ECG has been developed to potentially detect LVSD, which is commonly assessed by LVEF via echocardiography.

Currently, four AI-ECG tools are approved by the US Food and Drug Administration (FDA) to aid clinicians in classifying LVEF ≤40% (Table 1).[8-11] It should be noted that these AI-ECG tools are not meant to be standalone diagnostic tools, but to assist healthcare providers in assessing LVEF ≤40%, in conjunction with their own evaluation and clinical judgement. Of these, the Anumana ECG-AI LEF tool is locally available and has been registered with the Health Sciences Authority since June 2025.

Most AI-ECG tools are used to analyse 12-lead ECG signals, except for Eko ELEFT, which analyses single-lead ECG and phonocardiogram recorded by the Eko DUO digital stethoscope. Both Eko ELEFT and Anumana ECG-AI LEF are built upon the foundational Mayo Clinic's 12-lead ECG-based algorithm for detecting low LVEF, with retraining of the algorithm for the respective devices.

**Table 1: Summary of FDA-approved AI-ECG tools**

| Technology (Manufacturer); Year of FDA approval | Indication for use | Inputs | Outputs |
|---|---|---|---|
| Eko Low Ejection Fraction Tool (ELEFT; Eko Health Inc); 2024 | ELEFT is a software intended to aid clinicians in identifying individuals with left ventricular ejection fraction (LVEF) less than or equal to 40%. ELEFT takes as input ECG and heart sounds and is intended for use on patients at risk for heart failure This population includes, but is not limited to, patients with: coronary artery disease; diabetes | Single-lead ECG obtained from the Eko DUO digital stethoscope; may also analyse PCG signals when available. | • Normal EF<br>• Low EF<br>• Poor ECG signal |

| | | | |
|---|---|---|---|
| | mellitus; cardiomyopathy; hypertension; and obesity. | | |
| ECG-AI Low Ejection Fraction (LEF) 12-Lead Algorithm (Anumana, Inc.); 2023<br><br>Note: This technology is registered with the Health Sciences Authority (HSA) since June 2025 (DE0510824) for the same indication for use. | The ECG-AI LEF 12-Lead algorithm is software intended to aid in earlier detection of LVEF less than or equal to 40% in adults at risk for heart failure. This population includes, but is not limited to:<br>• patients with cardiomyopathies<br>• patients who are post-myocardial infarction<br>• patients with aortic stenosis<br>• patients with chronic atrial fibrillation<br>• patients receiving pharmaceutical therapies that are cardiotoxic, and<br>• postpartum women. | 12-lead ECG | • Low LVEF detected<br>• Low LVEF not detected<br>• Error |
| Tempus ECG-Low EF (Tempus AI, Inc.); 2025 | Tempus ECG-Low EF is software intended to analyse resting, non-ambulatory 12-lead ECG recordings and detect signs associated with having a low LVEF less than or equal to 40%). It is for use on clinical diagnostic ECG recordings collected at a healthcare facility from patients 40 years of age or older at risk of heart failure.<br>This population includes but is not limited to patients with atrial fibrillation, aortic stenosis, cardiomyopathy, myocardial infarction, diabetes, hypertension, mitral regurgitation, and ischemic heart disease. | | • Low LVEF detected<br>• Low LVEF not detected<br>• Unclassifiable |
| Bunkerhill ECG-EF (BunkerHill Health); 2025 | Bunkerhill ECG-EF is software intended to aid in screening for LVEF less than or equal to 40% in adults at risk for, but not already diagnosed with, low LVEF. | | • Low EF screen positive<br>• Low EF screen negative<br>• Error |
| Abbreviations: AI, artificial intelligence; ECG, electrocardiogram; PCG, phonocardiogram. | | | |

These AI-ECG tools may provide accessible and rapid LVEF detection for integration into routine point-of-care settings where echocardiography is not readily available. They offer the potential for healthcare practitioners to detect low LVEF in patients at risk of HF, facilitating early diagnosis in some patients. This allows prioritisation of high-risk patients for further interventions while potentially obviating costly tests for patients determined to have a low risk of HF.

## III. Subsidy Status

The Centers for Medicare and Medicaid Services (CMS) included AI-ECG technology in its 2025 Hospital Outpatient Prospective Payment System, allowing reimbursement for outpatient services involving AI-ECG tools with a Medicare rate of US$128.90 (S$175)[1] per assessment.[12]

## IV. Stage of Development in Singapore

☐ Yet to emerge ☐ Established

[1] Based on the Monetary Authority of Singapore exchange rate from 2024 to 2025: US$1=S$1.3603. Figures were rounded to the nearest dollar.

| | | | |
|---|---|---|---|
| ☒ | Investigational / Experimental (subject of clinical trials or deviate from standard practice and not routinely used) | ☐ | Established *but* modification in indication or technique |
| ☐ | Nearly established | ☐ | Established *but* should consider for reassessment (due to perceived no/low value) |

## V. Treatment Pathway

Based on the 2021 European Society of Cardiology (ESC) guideline for HF,[13] patients presenting with suspected HF should undergo a detailed clinical assessment that includes identification of risk factors (e.g. history of myocardial infarction, arterial hypertension, coronary artery disease, diabetes mellitus or chronic kidney disease), symptoms or signs (e.g. breathlessness, fatigue or ankle swelling), and ECG. For patients with symptoms and signs suggestive of HF, the measurement of plasma natriuretic peptide may aid diagnosis. Patients with N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration of ≥125ng/L or B-type natriuretic peptide ≥35 pg/mL should be referred for specialist assessment and transthoracic echocardiography (TTE) to determine the LVEF and subsequently the HF phenotype (Figure A1 in Appendix A).

Local clinician shared that if locally introduced, AI-ECG tools can be used as an adjunct after clinical assessment and before natriuretic peptide measurement. To illustrate, AI-ECG-derived LVEF ≤40% combined with an abnormal NT-proBNP level could help triage patients for fast-track echocardiography. Conversely, normal findings for both AI-ECG-derived LVEF and NT-proBNP would suggest that HF is unlikely, potentially avoiding echocardiography (Personal communication, Senior Consultant from Khoo Teck Puat Hospital, 31 October 2025).

## VI. Summary of Evidence

This assessment was conducted based on the Population, Intervention, Comparison and Outcome (PICO) criteria presented in Table 2. Literature search was conducted in PubMed, Embase, Cochrane Library, INAHTA database and manufacturer websites. The key evidence base comprises seven peer-reviewed publications: the SPEC-AI Nigeria and EAGLE randomised controlled trials (RCTs),[14, 15] four prospective observational studies,[16-19] and a cost-effectiveness study[20] based on post-hoc analysis of the EAGLE trial. Most study populations aligned with the PICO criteria, consisting primarily of patients undergoing a clinically indicated echocardiography, however the SPEC-AI Nigeria trial recruited pregnant or postpartum Nigerian women (n=1,195) and the EAGLE trial involved patients from a general screening population. The SPEC-AI Nigeria trial compared AI-guided screening of LVSD using the Eko and Anumana AI-ECG tools against standard 12-lead ECG with usual care.[14] The EAGLE trial evaluated primary care teams (n=358 clinicians) with and without access to results derived from an early version of Anumana ECG-AI LEF.[15] Both RCTs primarily focused on an

LVEF threshold of 50%, with outcomes for an LVEF threshold of 40% examined in subgroup analyses.[14, 15]

All key evidence investigated the Eko ELEFT and Anumana ECG-AI LEF algorithms only. No peer-reviewed evidence was identified for the other two FDA-approved AI-ECG tools. Given this, supporting clinical data submitted to the FDA for regulatory approval for Tempus ECG-Low EF[8] and Bunkerhill ECG-EF,[11] along with those for Eko ELEFT[9] and Anumana ECG-AI LEF,[10] were included as supplementary evidence. Additionally, a systematic review[21] that included the early foundational 12-lead ECG-based Mayo algorithm underpinning the Eko and Anumana AI-ECG tool was also presented as further supplementary evidence.

The evidence base, inclusion and exclusion criteria were listed in Table B1 (Appendix B), while the study design and characteristics of the included studies were presented in Table B2 (Appendix B).

**Table 2: PICO criteria**

| | |
|---|---|
| **Population** | Patients with suspected heart failure or who are referred to for LVEF assessment |
| **Intervention** | FDA-approved AI-ECG tools for LVEF assessment[a] |
| **Comparison** | Conventional LVEF assessment tools, including echocardiography as a reference standard |
| **Outcome** | Safety, clinical (accuracy, time to diagnosis, diagnostic yield, impact on clinical management such as GDMT initiation, HF hospitalisation and mortality) and cost effectiveness |

[a] All FDA-approved AI-ECG tools;Eko ELEFT, Anumana ECG-AI LEF, Tempus ECG-Low EF and Bunkerhill ECG-EF for detecting LVEF ≤40%.

Abbreviations: AI, artificial intelligence; AI-ECG, artificial intelligence-enhanced electrocardiography; ECG, electrocardiogram; FDA, US Food and Drug Administration; HF, heart failure; GDMT, guideline-directed medical therapy; LVEF, left ventricular ejection fraction.

## Safety

Based on findings from SPEC-AI Nigeria RCT, Eko ELEFT and Anumana ECG-AI LEF were found to be safe. No serious adverse events (SAEs) were reported, with five cases of skin irritation observed, arising from placement of ECG electrodes.[14] Compared to usual care, the use of either AI-ECG tool did not result in a significant difference in composite adverse events (AEs) that included HF, gestational hypertension, pre-eclampsia, gestational diabetes or any other pregnancy-related complication (odds ratio [OR], 1.00; 95% CI, 0.74 to 1.35; p=0.975).[14]

Other potential safety risks include health risks arising should algorithm or software failure impede clinical care, although this is not easily quantified.

## Effectiveness

*Accuracy*

Across three prospective observational studies[17-19] and the SPEC-AI Nigeria RCT,[14] Eko ELEFT and Anumana ECG-AI LEF demonstrated sensitivity of 76.5% to 100%, specificity of 78.3% to 97% and negative predictive value (NPV) of 98% to 100% for detecting LVEF ≤40% against echocardiography (Table 3). Notably, low positive predictive values (PPV) were reported (16.4% to 43.3%) which were attributed to the low prevalence of individuals with LVEF ≤40% in the study populations.[18, 19] It is important to note that while the three observational studies[17-19] included all patients clinically indicated for echocardiography, the RCT[14] included pregnant and postpartum women which may limit its generalisability.

Across the included studies, the Eko tool had the most supporting evidence, demonstrating moderate to good diagnostic performance (sensitivity, 77.5% to 100%; specificity, 78.3% to 81.8%; NPV, 98% to 100%), except for the reported PPV of 16.4% to 35.1%, when compared to echocardiography for detecting LVEF ≤40%.[14, 17-19] Subgroup analyses demonstrated consistent diagnostic performance across age, sex and ethnicity (see Figures C1 and C2 in Appendix C).[18, 19] Notably, Guo et al. (2025)[19] reported lower sensitivity (77.5%) and specificity (78.3%) compared to the other studies. The reason for this is not apparent but may be partially related to their larger multi-site cohort (n=2,960), which likely introduced greater heterogeneity into the study population. Additionally, Guo et al. (2025)[19] used a predetermined threshold to determine sensitivity and specificity, whereas some other studies optimised these thresholds based on their study dataset.[18]

One study of the Anumana AI-ECG tool showed similar diagnostic accuracy to Eko ELEFT, but achieved higher specificity (97%) and PPV (43.3%; Table 3).[14] While the Anumana tool has less direct published evidence in its current commercial form, multiple studies of the Mayo algorithm-based foundational 12-lead ECG upon which Anumana is based may provide additional support for its performance. The Mayo algorithm demonstrated an area under the receiving operator curve (AUROC) range of 0.83 to 0.97, sensitivity of 73% to 90% and specificity of 78% to 92% in identifying patients with LVEF ≤40% (see Table C1 in Appendix C).[21]

**Table 3: Diagnostic accuracy of AI-ECG tools with echocardiography as ground truth**

| Study[a] | N | AUROC (95% CI) | Sensitivity, % (95% CI) | Specificity, % (95% CI) | PPV, % (95% CI) | NPV, % (95% CI) |
|---|---|---|---|---|---|---|
| **Eko ELEFT** | | | | | | |
| Attia et al. (2022)[17] | 100 | 0.89 (0.83 to 0.96) | 87.5% (NR) | 80.4% (NR) | 28.0% (NR) | 98.7% (NR) |
| Bachtiger et al. (2022)[18] | 1,050 | 0.91 (0.88 to 0.95) | 91.9% (78.1% to 98.3%) | 80.2% (75.5% to 84.3%) | 35.1% (NR) | 98.4% (NR) |
| Adedinsewo et al. (2024)[14] | 587 | 0.99 (0.97 to 1.00) | 100.0% (83.2% to 100.0%) | 81.8% (78.3% to 84.9%) | 16.4% (10.3% to 24.2%) | 100.0% (99.2% to 100.0%) |
| Guo et al. (2025)[19] | 2,960 | 0.85 (0.83 to 0.88) | 77.5% (70.7% to 83.4%) | 78.3% (76.7% to 79.9%) | 20.3% (17.3% to 23.5%) | 98.0% (97.3% to 98.6%) |
| **Anumana ECG-AI LEF** | | | | | | |
| Adedinsewo et al. (2024)[14] | 587 | 0.93 (0.87 to 0.99) | 76.5% (50.1% to 93.2%) | 97.0% (95.2% to 98.2%) | 43.3% (25.5% to 62.6%) | 99.3% (98.1% to 99.8%) |

[a] All studies used ECG as input, except Guo et al. (2025) and Adedinsewo et al. (2024) which used both ECG and phonocardiogram (PCG) signals.

Abbreviations: AI-ECG, artificial intelligence-enhanced electrocardiography; AUROC, area under the receiving operator curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

Based on the submitted FDA data, Tempus ECG-Low EF and Bunkerhill ECG-EF reported comparable diagnostic performance as Eko ELEFT and Anumana ECG-AI LEF, though these preliminary findings await validation through peer-reviewed publications (Table 4).[8-11] It is worth noting that, similar to Guo et al. (2025), Eko ELEFT demonstrated lower sensitivity (74.7% *vs.* 82.7% to 86%) and specificity (77.5% *vs.* 83% to 83.6%) compared to the other

tools. It is not clear whether this may be partly due to it being a single-lead rather than a 12-lead tool.

**Table 4: Supporting accuracy data of AI-ECG tools submitted to the FDA**

| FDA approval document | N | Sensitivity, % (95% CI) | Specificity, % (95% CI) | PPV, % (95% CI) | NPV, % (95% CI) |
|---|---|---|---|---|---|
| K233409 (Eko ELEFT)[9 10] | 3,456 | 74.7% (69.4% to 79.6%) | 77.5% (75.9% to 79.0%) | — | — |
| K232699 (Anumana ECG-AI LEF)[10] | 16,000 | 84.5% (82.2% to 86.6%) | 83.6% (83.0% to 84.3%) | 30.4% (28.8% to 32.1%) | 98.5% (98.2% to 98.7%) |
| K250119 (Tempus ECG-Low EF)[8] | >15,000[a] | 86% (84% to NR) | 83% (82% to NR) | 38% (NR) | 98% (NR) |
| K250649 (Bunkerhill ECG-EF)[11] | 15,994 | 82.7% (80.9% to 84.3%) | 83.2% (82.6% to 83.8%) | 37.2% (35.7% to 38.8%) | 97.5% (97.3% to 97.8%) |

[a] Refer to number of electrocardiograms.

Abbreviations: AI-ECG, artificial intelligence-enhanced electrocardiography; CI, confidence interval; FDA, US Food & Drug Administration ; NPV, negative predictive value; NR, not reported; PPV, positive predictive value.

*Clinical Utility*

Findings from the EAGLE RCT showed that compared to usual care, the use of Anumana ECG-AI LEF did not result in significant changes in the detection of low LVEF (≤40%) or clinical management.[15] While a numerically higher proportion of patients managed by clinicians with access to the AI-ECG results had lower LVEF detected than those in the control group, this difference did not reach statistical significance (0.9% vs. 0.6%, p=0.057; Table 5).[15] Similarly, no significant between-group difference was observed in the use of guideline-recommended medications (Table 6).[15]

**Table 5: Impact of Anumana ECG-AI LEF on the detection of low LVEF**

| LVEF threshold | Intervention, n/N (%)[a] | Control, n/N (%)[b] | OR (95% CI) | p-value |
|---|---|---|---|---|
| ≤40% | 102/11,573 (0.9%) | 70/11,068 (0.6%) | 1.39 (0.99 to 1.95) | 0.057 |

[a] Clinicians in the intervention group had access to AI-ECG results.

[b] Clinicians in the control group had no access to AI-ECG results.

Abbreviations: CI, confidence interval; LEF, low ejection fraction; LVEF, left ventricular ejection fraction; OR, odds ratio.

Table adapted from Yao et al. (2021).[15]

**Table 6: Impact of Anumana ECG-AI LEF on guideline-directed medical therapy**

| Use of guideline-recommended medications | Intervention[a] (n=102) | Control[b] (n=70) | p-value |
|---|---|---|---|
| **Baseline use[c], n (%)** | | | |
| ACEi/ARB or beta blockers | 60 (58.8%) | 32 (45.7%) | 0.090 |
| ACEi/ARB | 45 (44.1%) | 21 (30.0%) | 0.061 |
| Beta blockers | 30 (29.4%) | 24 (34.3%) | 0.499 |
| **New prescription[d], n (%)** | | | |
| ACEi/ARB or beta blockers | 74 (72.5%) | 52 (74.3%) | 0.800 |
| ACEi/ARB | 44 (43.1%) | 37 (52.9%) | 0.210 |
| Beta blockers | 65 (63.7%) | 38 (54.3%) | 0.215 |

[a] Clinicians in the intervention group had access to AI-ECG results.

[b] Clinicians in the control group had no access to AI-ECG results.

[c] Baseline use of ACEi, ARB, and beta blocker were determined based on prescription records within the past 12 months.

[d] New prescriptions were defined as patients who did not have a prescription at a baseline but received one during the 90-day follow up.

Abbreviations: ACEi, angiotensin-converting-enzyme inhibitors; AI-ECG, artificial intelligence-enhanced electrocardiography; ARB, angiotensin II receptor blocker.

Table adapted from Yao et al. (2021).[15]

Findings from the SPEC-AI Nigeria RCT demonstrated that the Eko and Anumana AI-ECG tools did not result in significant differences in cardiovascular-related events and mortality rates compared to usual care.[14] Across both groups, no significant differences in composite cardiovascular events (OR, 1.10; p=0.621) or cardiovascular-related mortality (hazard ratio [HR], 1.75; p=0.442) were reported (Table 7).[14] However, the intervention arm showed significantly higher all-cause mortality (HR, 4.20; 95% CI, 1.18 to 14.87; p=0.026), which was attributed to non-cardiovascular causes, including renal failure, infections, and other unknown causes.[14] The authors suggested this finding may reflect differential observation or reporting between the groups. The applicability of these findings to the general population remains limited, given potential differences in cardiovascular physiology and risk factors between the populations.

**Table 7: Impact of Eko and Anumana AI-ECG tools on clinical outcomes**

| Outcome | Intervention (n=587)[a,c] | Control (n=608)[b,c] | Effect estimate (95% CI)[d] | p-value |
|---|---|---|---|---|
| Composite cardiovascular events[e] | 9.5% (56/587) | 8.7% (53/608) | OR, 1.10 (0.74 to 1.64) | 0.621 |
| All-cause mortality | 2.0% (12/587) | 0.5% (3/608) | HR, 4.20 (1.18 to 14.87) | **0.026** |
| Cardiovascular mortality | 0.9% (5/587) | 0.5% (3/608) | HR, 1.75 (0.42 to 7.33) | 0.442 |

Notes:

[a] Patients in the intervention group received 12-lead ECG, portable ECGs recorded with a digital stethoscope with binary AI predictions for LVSD (positive or negative), 12-lead AI-ECG binary prediction for LVSD (positive or negative), and confirmatory echocardiogram at baseline.

[b] Patients in the control group received 12-lead ECG with standard care.

[c] Patients were followed up through 12 months post-partum or study end, whichever was earlier.

[d] Effect estimates reported were unadjusted.

[e] Composite cardiovascular events include diastolic heart failure, gestational hypertension, pre-eclampsia, eclampsia, valvular heart disease, atrial arrhythmias and sustained ventricular arrhythmias.

Abbreviations: AE, adverse event; AI, artificial intelligence; AI-ECG, artificial intelligence-enhanced electrocardiography; CI, confidence interval; ECG, electrocardiogram; HR, hazard ratio; LVSD, left ventricular systolic dysfunction; OR, odds ratio.

Table adapted from Adedinsewo et al. (2024).[14]

Moreover, findings from one prospective observational study demonstrated that the Eko ELEFT tool could potentially predict patients at risk of major adverse cardiovascular events (MACE) and all-cause mortality at two-year follow-up, independent of actual LVEF measured by echocardiography.[16] When analysed using these Eko ELEFT predictions, low LVEF detection showed significant associations with MACE and all-cause mortality in multivariable regression analysis adjusted for other clinical variables (MACE: HR, 1.93, p=0.0001; all-cause mortality: HR, 1.56, p=0.024; see Table C2 in Appendix C).[16]

**Cost effectiveness**

A cost-effectiveness analysis (CEA) of the EAGLE RCT indicated that AI-ECG (Anumana) was cost-effective in screening for low LVEF in patients without signs or clinical diagnosis of HF who underwent a clinically indicated ECG. The CEA was based on a lifetime Markov model from the healthcare payer perspective with a 3% discount rate. Key assumptions included patients at baseline being at the same health level as the general population, TTE as the gold standard for diagnosis, and all diagnosed patients receiving guideline-directed therapy.[20]

Compared to usual care, the base case analysis yielded an incremental cost-effectiveness ratio (ICER) of US$27,858 (S$37,895)[a] per quality-adjusted life year (QALY).[20] Despite modest short-term clinical improvements in the EAGLE trial, where AI-ECG showed a non-significant increase in low LVEF detection (0.9% *vs.* 0.6%), the favourable ICER may be attributed to the lifetime Markov model's projection of long-term benefits from early detection and treatment. One-way sensitivity analyses revealed that the model was most sensitive to the cost of AI-ECG screening (see Figure C3 in Appendix C).

Scenario analyses demonstrated that cost-effectiveness varied across different patient populations and settings. When examining only patients flagged as AI-ECG positive, the intervention demonstrated a substantially greater health benefit (2.19 QALYs gained *vs.* 0.014 in the base case), resulting in enhanced cost-effectiveness (ICER: US$23,435 [S$31,879][a] per QALY). The intervention was most cost-effective in younger patients, in outpatient settings, and among patients with underlying low EF (Table 8).[20] Cost-effectiveness improved with longer follow-up duration, with ICER decreasing from US$35,698 (S$48,553)[a] per QALY at 10 years to US$27,858 (S$37,895)[a] per QALY at 50 years .[20]

Probabilistic sensitivity analysis of 1,000 simulations indicated that AI-ECG was cost-effective 79.5% of the time at a willingness-to-pay (WTP) threshold of US$100,000 (S$136,030)[a] per QALY, with the intervention being the preferred strategy when the WTP threshold exceeded US$27,500 (S$37,408)[a] per QALY.[20]

**Table 8: Cost-effectiveness of AI-ECG (Anumana) compared to usual care[a]**

| Cohort | ICER (US$ per QALY) |
|---|---|
| **Base case analysis** | 27,588 |
| **Scenario analysis (AI-ECG positive only)** | 23,435 |
| **Scenario analysis (Underlying low EF)** | 13,136 |
| **Scenario analysis (Follow-up time)** | |
| 10 years | 35,698 |
| 20 years | 30,095 |
| 50 years | 27,858 |
| **Scenario analysis (Age)** | |
| 20 years old | 13,007 |
| 80 years old | 36,213 |
| **Scenario analysis (Outpatient setting)** | 1,651 |

[a] Intervention comprises standard 12-lead ECG and AI-ECG (Anumana) results that were both shared with clinicians. Usual care comprises standard 12-lead ECG and AI-ECG (Anumana), of which only the ECG results were shared with clinicians.

Abbreviations: AI-ECG, artificial intelligence-enhanced electrocardiography; ECG, electrocardiogram; EF, ejection fraction; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Table adapted from Thao et al. (2024).[20]

## Ongoing trials

Three ongoing studies were identified from the ScanMedicine database (NIHR Innovation Observatory; Table 9). Two of these studies, comprising an RCT and a prospective observational study, are evaluating the impact of Eko ELEFT on clinical and system-level outcomes, with expected completion by December 2025. Additionally, the Tempus ECG-Low EF tool is being investigated in a separate RCT examining low LVEF detection and patient health outcomes. It should be noted that the trial is indicated as not yet recruiting, with an estimated completion date of February 2026.

No ongoing trials were identified for Anumana ECG-AI LEF and Bunkerhill ECG-EF.

**Table 9: Ongoing clinical trials**

| AI-ECG tool | Study (Trial ID) | Estimated enrolment | Brief description | Estimated completion date |
|---|---|---|---|---|
| Eko ELEFT | TRICORDER (NCT05987670) | 200[a] | A cluster RCT to evaluate the clinical and cost-effectiveness of providing primary care teams with the AI-stethoscope for the detection of heart failure, assessing its impact on overall detection of heart failure, low LVEF detection, and healthcare system cost. | December 2025<br>Current status: Active, not recruiting |
| | PLANE-HF (NCT05817136) | 80 | A prospective observational study to evaluate the use of the Eko AI-ECG as a self-monitoring programme for patients with newly diagnosed heart failure to evaluate its impact on LV impairment, medication optimisation and healthcare episodes. | June 2024<br>Current status: Unknown |
| Tempus ECG-Low EF | NOTABLE (NCT06511505) | 1,000 | A RCT to compare the rates of new disease diagnoses, therapeutic interventions, and cardiovascular outcomes between healthcare providers with and without access to AI-ECG results. | February 2026<br>Current Status: Not yet recruiting |

[a] Sample size refers to primary care practices recruited in the trial. Based on a media report, TRICORDER spanned 205 NHS GP practices with 1.5 million registered patients, including more than 12,800 AI-stethoscope exams performed by nearly 1,000 providers.[22]

Abbreviations: AI-ECG, artificial intelligence-enhanced electrocardiography; ECG, electrocardiogram; EF, ejection fraction; LVEF, left ventricular ejection fraction; RCT, randomised controlled trial.

**Summary**

Based on published evidence available for Eko ELEFT and Anumana ECG-AI LEF, AI-ECG tools demonstrated acceptable safety profiles and diagnostic accuracy for detecting LVEF ≤40%. No SAEs were reported with the use of the Eko and Anumana tools, with similar composite AE reported for AI-ECG and usual care (OR, 1.00; p=0.975). Across the two AI-ECG tools, moderate to good accuracy (overall sensitivity, 76.5% to 100%; specificity, 78.3% to 97%; NPV, 98% to 100%) was demonstrated in distinguishing LVEF ≤40% when compared to echocardiography, although a low PPV was reported (16.4% to 43.3%). Limited data suggest that the Anumana tool appeared to perform better than Eko in terms of specificity (97% *vs.* 78.3% to 81.8%) and PPV (43.3% *vs.* 16.4% to 35.1%). For the Tempus ECG-Low EF and Bunkerhill ECG-EF tools, no additional studies were identified other than data submitted to the FDA, which showed comparable diagnostic performance to the other AI-ECG tools.

Evidence for clinical utility remains limited. The Anumana tool showed minimal impact on the detection of low LVEF (0.9% vs. 0.6%, p=0.057) and did not significantly alter guideline-directed medical therapy compared to usual care. Results for the Eko ELEFT tool suggested

potential prognostic value independent of LVEF diagnosis, with predicted low LVEF showing significant associations with MACE (HR, 1.93; p=0.0001) and all-cause mortality (HR, 1.56; p=0.024) in multivariate analysis.

Compared to usual care, both the Eko and Anumana tools showed similar composite cardiovascular events (OR, 1.10; p=0.621) and cardiovascular-related mortality (HR, 1.75; p=0.442). However, the generalisability of these findings is unclear as they are limited to pregnant and postpartum women. A cost-effectiveness analysis indicated the Anumana tool was cost-effective with an ICER of US$27,858 per QALY compared to usual care, particularly in outpatient settings (US$1,651 per QALY).

These findings need to be interpreted with caution. In some studies (e.g. the SPEC-AI Nigeria trial), echocardiograms were not performed in the control group. Additionally, while the study protocol advised repeat echocardiography for positive AI-ECG results in the intervention group, this remained at the clinician's discretion. The lack of standardised LVEF assessment with echocardiography may affect diagnostic accuracy results. Moreover, potential inter-operator variability in LVEF assessment and ECG lead positioning may cause misclassification of borderline cases near the 40% threshold, further affecting diagnostic accuracy. Evidence on the long-term impact of AI-ECG tools on clinical outcomes, including HF hospitalisation, mortality and clinical management, remains limited. Additionally, there was an under-representation of Asian patients in the evidence base (range, 0% to 19.9%), which may limit generalisability to the local population.

## VII. Estimated Costs

No cost information was identified for AI-ECG tools. Of note, the cost-effectiveness study assumed the cost of an AI-ECG analysis to be US$100 (S$136)[a].[20]

## VIII.Implementation Considerations

The adoption of AI-ECG tools faces several implementation challenges. Clinician buy-in remains a key challenge, often stemming from concerns about trust in automated interpretations and the opaque nature of AI algorithms.[23] Training is important not only to familiarise clinicians with the technical aspect of AI-ECG tools, but also to equip them with skills to effectively communicate the confidence levels and limitations of low LVEF risk predictions to patients. There is also a risk that a paternalistic model of medical decision-making could emerge, where clinicians over-rely on AI outputs without fully engaging patients in the process.[24]

Clinical governance presents additional complexities, such as determining who holds accountability for decisions influenced by AI, maintaining quality oversight, and ensuring cybersecurity and data privacy. The Ministry of Health (MOH) Artificial Intelligence in Healthcare Guidelines (AIHGle) emphasises that clinical governance and oversight are required for safe and responsible implementation.[25] This includes obtaining relevant organisational approvals, proper documentation of the AI implementation decisions,

conducting risk assessment to anticipate potential software failures, and establishing mitigation measures such as reverting to echocardiography for LVEF assessment when necessary. Proper implementation also requires understanding how AI-ECG tools fit within local clinical practice, ensuring the AI training dataset is representative of the local patient populations, and establishing performance tracking systems to verify that tools maintain manufacturer-specified performance levels through ground-truthing. For cloud-based AI-ECG tools, adequate cybersecurity measures should be in place to protect against and respond to digital threats and vulnerabilities.

Additionally, proper workflow integration is crucial to ensure that AI-ECG results are integrated seamlessly into clinical workflows without causing disruption or excessive administrative burden.[23] This includes ensuring compatibility with electronic health record systems and adapting to varied clinical environments where these tools may be deployed. For Eko ELEFT specifically, adoption would require clinicians to transition from a traditional analogue stethoscope to a digital ECG-enabled one. At the same time, high-quality standardised digital ECG acquisition is needed as input for AI-ECG tools.

While AI-ECG tools promise to enable timely referral of patients with low LVEF for confirmatory echocardiogram scans, this may inadvertently increase imaging volumes and potentially delay care for patients with more urgent needs.[23] Successful adoption may therefore require developing additional triage strategies to prevent overwhelming existing imaging resources and compromising patient care. This necessitates ongoing monitoring of referral patterns and imaging wait times, along with flexible resource allocation such as increasing echocardiography capacity to maintain timely and equitable access to diagnostic services. Continuous monitoring of the clinical impact of AI-ECG-guided referrals is essential to ensure that increased detection of low LVEF translates to improved patient outcomes without straining healthcare resources or introducing inefficiencies in the care pathways.

## IX. Concurrent Developments

Aside from AI-ECG tools that have received FDA clearance to detect for low LVEF, several other comparable commercial software solutions have been approved in Europe or South Korea (Table 10). Additional research-use-only algorithms are currently under development.[21] There are also AI tools designed to detect multiple structural heart diseases, including low LVEF, with at least one such device approved in Europe (Table 10).

Other novel uses of AI tools to interpret ECG readings are also rapidly emerging, allowing the identification of various cardiac conditions such as atrial fibrillation, hypertrophic cardiomyopathy and arrythmia.[26]

**Table 10: Ongoing development of AI-ECG algorithms for low LVEF detection**

| Technology (Manufacturer) | Brief description | Status |
|---|---|---|
| **Detection of low LVEF only** | | |
| AiTiALVSD (Medical AI Co., Ltd.) | The software as a medical device analyses 12-lead ECG data using artificial intelligence to indicate the likelihood of LVSD with scores and risk assessment. | CE marked; regulatory approval in South Korea |

| | | |
|---|---|---|
| PMcardio LVsense (Powerful Medical) | The software offers a rapid assessment of left ventricular systolic function by detecting reduced LVEF from a 12-lead ECG. | CE marked |
| **Multi-condition detection, including low LVEF** | | |
| Cardio-HART (Cardio-Phoenix) | Cardio-HART is a next-generation ECG device that combines novel biosignals – heart sounds and chest wall motion – with AI to deliver diagnostic capabilities to derive outputs including LVEF, mitral and aortic regurgitation grade, LV mass and interventricular septum thickness. | CE marked |
| rECHOmmend (Tempus and Geisinger) | A novel ECG-based machine learning approach to predict multiple structural heart conditions. | For research use only |
| EchoNext (Columbia University) | A deep learning ECG model that can accurately detect a broad array of structural heart diseases. | For research use only |
| Abbreviations: AI-ECG, artificial intelligence-enhanced electrocardiography; CE, Conformité Européenne; ECG, electrocardiogram; LV, left ventricle; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction. | | |

## X. Additional Information

Local clinicians across the three public healthcare clusters identified a clear clinical need for AI-ECG tools, particularly for early detection and triage of LVSD. A key challenge highlighted was the late detection of patients with LVSD, who are often only identified after hospitalisation for HF.

The clinicians shared that AI-ECG tools would be valuable for upstream screening, to detect previously unrecognised LVSD in high-risk but asymptomatic patients, including those with diabetes, chronic kidney disease, hypertension and coronary artery disease. Additionally, AI-ECG would be useful for patients presenting with vague symptoms such as chest pain or shortness of breath who are undergoing clinically indicated ECG examination in primary care settings, allowing screening of low LVEF and facilitating earlier cardiology review when indicated. Given the high utilisation of echocardiography services with wait times extending to several months for non-urgent referrals, AI-ECG was also viewed as a valuable triage tool to prioritise patients with a high likelihood of LVEF ≤40% for echocardiography, thereby optimising resource allocation and reducing time to diagnosis.

Primary care settings, particularly polyclinics that conduct routine ECGs during chronic disease reviews, were identified as promising deployment sites where AI-ECG could offer opportunistic screening for high-risk patients, supporting Healthier SG's preventive care and risk-stratification goals. Early confirmation of HF in the community may allow timely guideline-directed medical therapies to be used. In particular, patients with early HF may be discharged to the community (e.g. primary care network clinics) and monitored by AI-ECG for deterioration below a set threshold for cardiologist review, facilitating safer shared care arrangements.

However, clinicians noted limitations of current approved AI-ECG systems, which provide threshold cut-offs but may not be useful for monitoring improvement or worsening over time. An echocardiogram will still be needed to confirm a diagnosis of HF, to provide comprehensive assessment and guide ongoing management.

Emergency departments were also highlighted as valuable implementation sites, with potential for expansion to other clinical areas such as diabetic clinics and non-cardiac

inpatient wards once cost-effectiveness is established and the AI-ECG tools reach sufficient maturity for widespread scaling (Personal communications, Senior Consultant, from Changi General Hospital, 28 October 2025 and 2 January 2026; Senior Consultant from Khoo Teck Puat Hospital, 31 October 2025 and 2 January 2026; Senior Consultant from National University Heart Centre Singapore, 31 October 2025 and 14 January 2026).

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# Appendix

## Appendix A: Clinical pathway for the diagnosis of patients suspected of heart failure

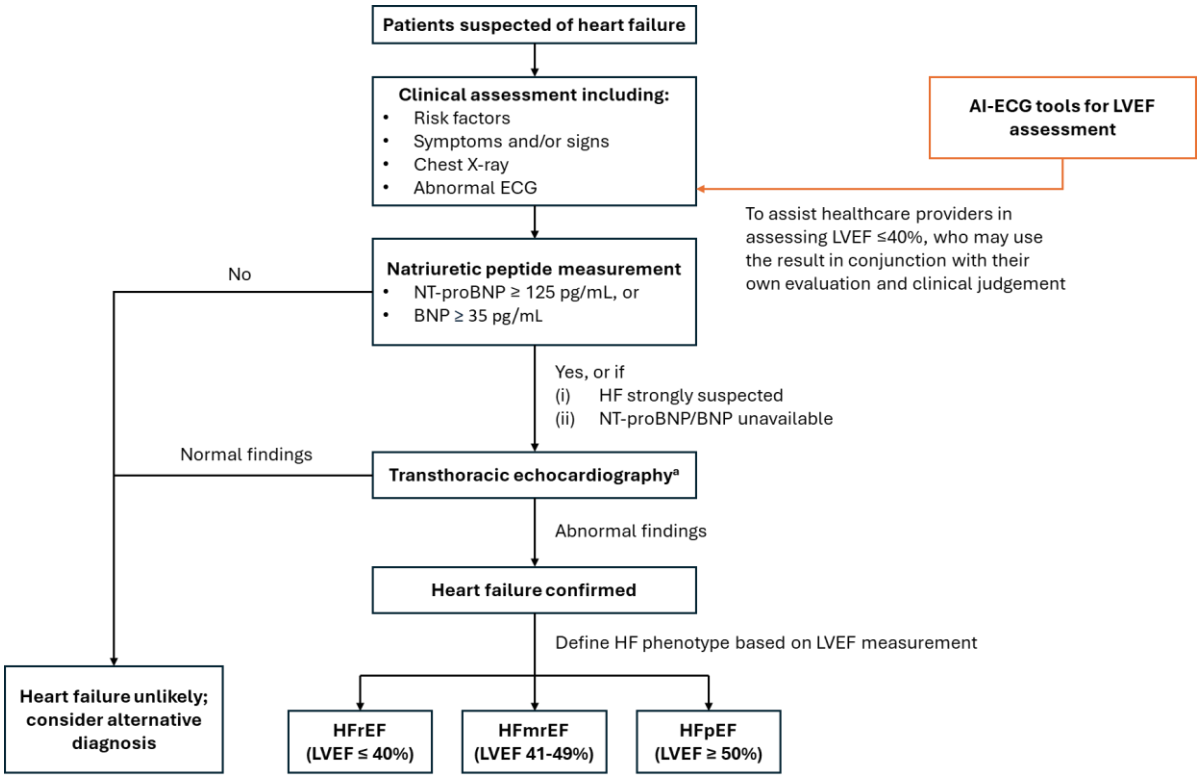


**Figure A1: Diagnostic algorithm for patients suspected of heart failure.** Adapted from the 2021 European Society of Cardiology Guidelines for the diagnosis and treatment of acute and chronic heart failure.

Note:

[a] In certain situations, echocardiogram may be unable to accurately assess cardiac structure or function, or more information is needed to determine the cause of the cardiac dysfunction. Other imaging modalities, such as CMR, SPECT or radionuclide ventriculography, PET, or cardiac CT or invasive coronary angiography, can provide additional and complementary information to cardiac ultrasound.

Abbreviations: BNP, B-type natriuretic peptide; CMR, cardiac magnetic resonance; CT, computed tomography; ECG, electrocardiogram; ELEFT, Eko Low Ejection Fraction Tool; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PCG, phonocardiogram; PET, positron emission tomography; SPECT, single-photon emission computerised tomography.

## Appendix B: Studies identified and study design

**Table B1: List of included studies**

| Type of studies | Key evidence | Supplementary evidence |
|---|---|---|
| Randomised controlled trial | 2 | — |
| Prospective observational study | 4 | — |
| Cost-effectiveness study | 1 | — |
| Systematic review | — | 1 |
| FDA 510(k) clearance summary | — | 4 |

Note:

1. Inclusion criteria
   a. Studies that fulfil the PICO criteria listed in Table 2.
2. Exclusion criteria
   a. Studies only available in the abstract form.

**Table B2: Characteristic of included studies**

| Study | Study design | Population (N) | Intervention | Comparator | Reference standard | Time between AI-ECG and confirmatory echo |
|---|---|---|---|---|---|---|
| **Key evidence** | | | | | | |
| Adedinsewo et al. (2024)[14] | RCT (SPEC-AI Nigeria) | Females aged 18 to 49 years, pregnant or within 12 months postpartum (n=1,195)<br><br>Asians enrolled: 0% | Eko ELEFT; Anumana ECG-AI LEF | 12-lead ECG + usual care | Echo | Not reported |
| Yao et al. (2021)[15] | RCT (EAGLE) | Primary care clinicians, including physicians, nurse practitioners and physician assistants, that cared for adult patients aged 18 years and above with no clinical history or diagnosis of HF (n=358)[a]<br><br>Asians enrolled: 1.2%<br><br>Population comprises 53.1% from outpatient clinic, 37.4% from emergency | Anumana ECG-AI LEF | Usual care | Echo | 8 days (median) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | department and 9.5% from hospital. | | | | |
| Bachtiger et al. (2022) | Prospective observational study | Adults (≥ 18 years) attending for transthoracic echocardiography (n=1,050)<br><br>Asians enrolled: 19% | Eko ELEFT | — | Echo | 24 hours |
| Attia et al. (2022)[17] | Prospective observational study | Patients referred for outpatient transthoracic echocardiography for any indication (n=100)<br><br>Asians enrolled: Not reported | Eko ELEFT | — | Echo | Immediate |
| Guo et al. (2025)[19] | Prospective observational study | Adults (≥ 18 years) undergoing a clinically indicated echocardiogram for any reasons (n=2,960)<br><br>Asians enrolled: 0.71% | Eko ELEFT | — | Echo | Within 7 days |
| Alrumayh et al. (2025)[16] | Prospective observational study | Patients attending for routine transthoracic echocardiogram (n=1,007)<br><br>Asians enrolled: 19.9%<br><br>Population comprises 36.1% from inpatient clinic and 63.9% outpatient clinic. | Eko ELEFT-derived LVEF ≤40% | Eko ELEFT-derived LVEF >40% | — | — |
| Thao et al. (2024)[20] | Cost-effectiveness study (post-hoc of EAGLE RCT) | Adults (≥ 18 years) with no clinical history or diagnosis of HF<br><br>Asians enrolled: 1.2% | Standard 12-lead ECG and AI-ECG from Anumana ECG-AI LEF, both results shared with clinician | Standard 12-lead ECG and AI-ECG from Anumana ECG-AI LEF, only ECG results shared with clinician | — | — |
| **Supplementary evidence** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Bjerkén et al. (2023)[21] | Systematic review | Studies investigating the use of AI-ECG to screen for reduced LVEF or LVSD (n=4)[b]<br><br>Asians enrolled: Not reported | — | — | — | — |
| FDA (Eko ELEFT; K233409)[9] | Not reported (results based on proprietary database) | Adults over the age of 18 with paired ECG and heart sound recordings and echocardiograms (n=3,456)<br><br>Asians enrolled: 15% | Eko ELEFT | — | Echo | Within 7 days |
| FDA (Anumana ECG-AI LEF; K232699)[10] | Retrospective observational study | Age ≥ 18 and the availability of at least one digital 12-lead ECG paired with an echocardiogram with quantitative LVEF information within 30 days following the date of the ECG (n=16,000)<br><br>Asians enrolled: 2.2% | Anumana ECG-AI LEF | — | Echo | Within 30 days |
| FDA (Tempus ECG-Low EF; K250119)[8] | Retrospective observational study | Population not defined (n>15,000)[c]<br><br>Asians enrolled: 2% | Tempus ECG-Low EF | — | Echo | Within 30 days |
| FDA (Bunkerhill ECG-EF; K250649)[11] | Retrospective observational study | Population not defined (n=15,994)<br><br>Asians enrolled: 3.9% | Bunkerhill ECG-EF | — | Echo | Within 15 days |

[a] Refers to the number of clinicians recruited in the EAGLE RCT. The analysis was based on a total of 22,641 patients.

[b] Four out of 15 studies included in the systematic review that used a LVEF threshold of 40% were included in this brief.

[c] Refers to the number of ECG.

Abbreviations: AI, artificial intelligence; ECG, electrocardiogram; ELEFT, Eko Low Ejection Fraction Tool; HF, heart failure; LEF, low ejection fraction; LVEF, left ventricular ejection fraction; LVSD, left ventricular systolic dysfunction; RCT, randomised controlled trial.

## Appendix C: List of supplementary tables and figures

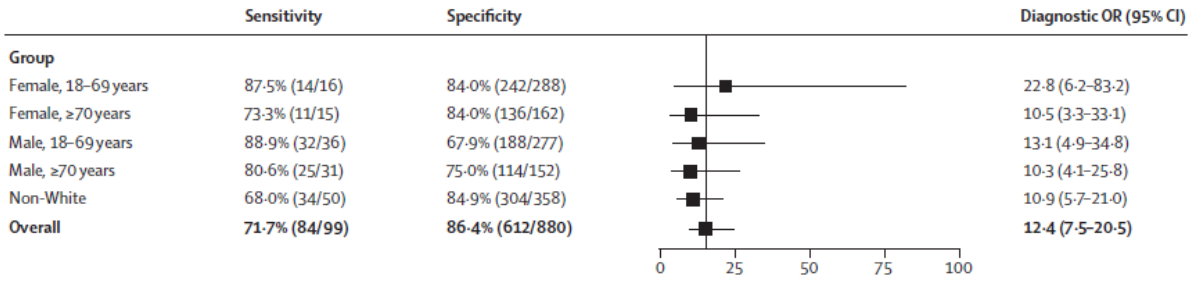


**Figure C1: Subgroup analysis of Eko ELEFT.** Figure adapted from Bachtiger et al. (2022).[18]

| | Recordings | Sensitivity | Specificity | PPV | NPV | Diagnostic Yield |
|---|---|---|---|---|---|---|
| Biological sex | | | | | | |
| Male | 1,451 | 79.5 (71.0-86.4) | 74.4 (71.8-76.8) | 23.5 (19.4-28.0) | 97.3 (96.1-98.3) | 89.5 (87.8-91.1) |
| Female | 1,509 | 73.8 (60.9-84.2) | 81.9 (79.7-83.9) | 15.8 (11.8-20.6) | 98.5 (97.6-99.2) | 91.8 (90.3-93.1) |
| Age (y) | | | | | | |
| 18-30 | 94 | 100 (15.8- nan) | 87.1 (78.0-93.4) | 15.4 (1.9-45.4) | 100 (95.1-nan) | 92.6 (85.3-97.0) |
| 31-50 | 400 | 68.8 (41.3-89.0) | 87.0 (83.1-90.4) | 19.3 (10.0-31.9) | 98.4 (96.3-99.5) | 92.7 (89.8-95.1) |
| 51-70 | 1,274 | 73.6 (61.9-83.3) | 81.6 (79.2-83.9) | 20.9 (16.0-26.4) | 97.9 (96.8-98.7) | 91.4 (89.8-92.9) |
| >70 | 1,192 | 81.8 (72.2-89.2) | 70.7 (67.7-73.6) | 20.2 (16.1-24.7) | 97.7 (96.3-98.7) | 89.0 (87.1-90.7) |
| Race | | | | | | |
| Black/African American | 748 | 72.2 (58.4-83.5) | 78.6 (75.2-81.8) | 22.7 (16.6-29.7) | 97.0 (95.1-98.3) | 90.4 (88.0-92.4) |
| White | 2,011 | 81.7 (73.1-88.4) | 77.4 (75.4-79.4) | 18.6 (15.2-22.4) | 98.5 (97.7-99.1) | 91.0 (89.7-92.3) |
| Other | 147 | 64.3 (35.1-87.2) | 85.3 (77.6-91.2) | 34.6 (17.2-55.7) | 95.2 (89.1-98.4) | 88.4 (82.1-93.1) |
| Asian | 21 | 100.0 (2.5-NA) | 88.2 (63.6-98.5) | 33.3 (0.8-90.6) | 100.0 (78.2-NA) | 85.7 (63.7-97.0) |
| American Indian or Alaska Native | 28 | - | 92.3 (74.9-99.1) | 0.0 (NA-84.2) | 100.0 (85.8-NA) | 92.9 (76.5-99.1) |

**Figure C2: Subgroup analysis of Eko ELEFT.** Figure adapted from Guo et al. (2025).[19]

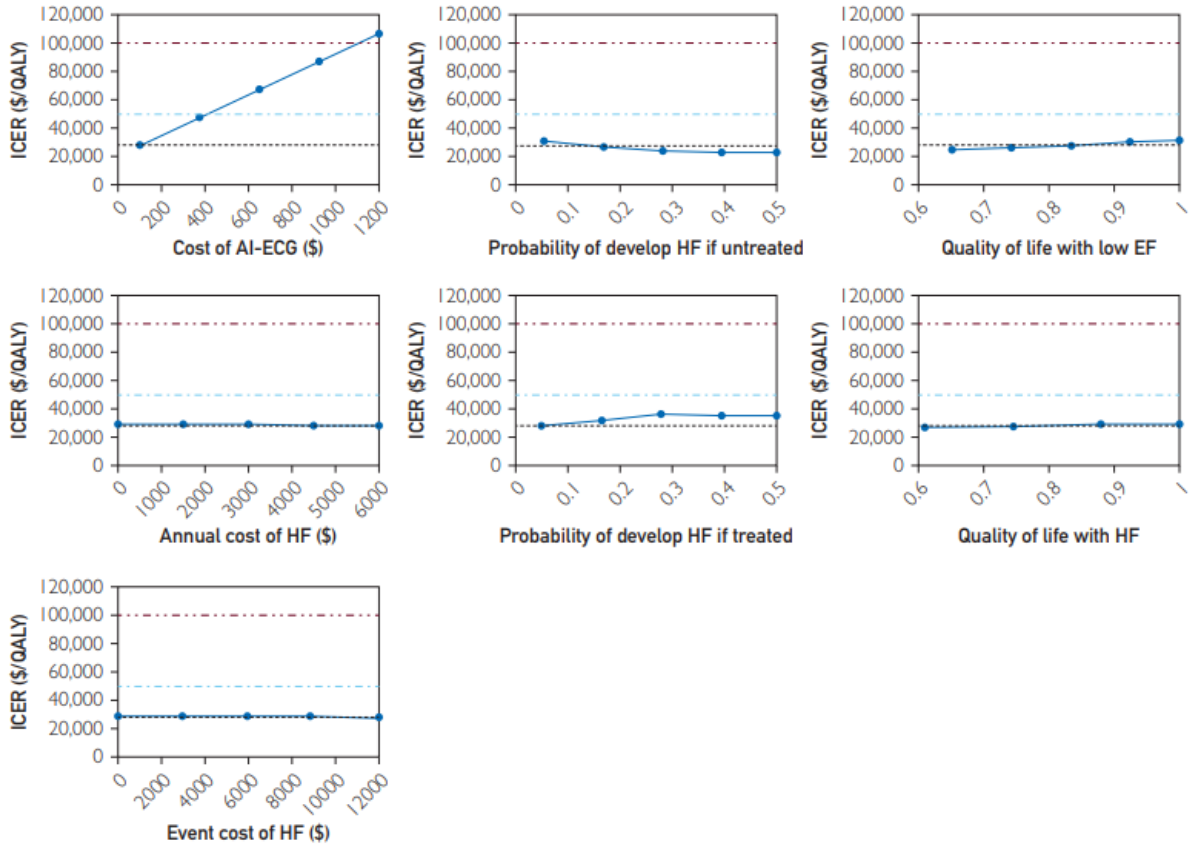


**Figure C3: Results from one-way sensitivity analysis of the Markov model examining cost-effectiveness of AI-ECG (Anumana) compared to usual care.** Red dashed line, WTP of $100,000; Green dashed line, WTP of $50,000; Purple dashed line, base-case incremental cost-effectiveness ratio.

Abbreviations: AI-ECG, artificial intelligence integrated electrocardiogram; EF, ejection fraction; HF, heart failure; ICER, incremental cost-effectiveness ratios; QALY, quality-adjusted life years; WTP, willingness-to-pay.

Figure adapted from Thao et al. (2024).[20]

**Table C1: Diagnostic accuracy of Mayo algorithm for detecting LVEF ≤40%**

| Study | Study design | Population | N | AUROC | Sensitivity | Specificity |
|---|---|---|---|---|---|---|
| Attia et al. | Retrospective cohort | Patients with Covid-19 with ECG and echocardiogram taken within 2 weeks | 27 | 0.95 | NR | NR |
| Jentzer et al. | Retrospective cohort | Patients in cardiac ICU with ECG and echocardiogram taken within 7 days | 5,680 | 0.83 | 73% | 78% |
| Kashou et al. | Prospective cohort | People who underwent ECG and echocardiogram on the same day | 2,041 | 0.97 | 90% | 92% |
| Brito et al. | Prospective cohort | Patients with Chagas disease who had ECG and echocardiogram performed | 1,304 | 0.84 | 73% | 83% |

Abbreviations: AUROC, area under the receiving operator curve; ECG, electrocardiogram; ICU, intensive care unit.
Data adapted from Bjerken et al. (2023).[21]

**Table C2: Multivariable Cox regression analysis of MACE and all-cause mortality**

| Variables | MACE | | All-cause mortality | |
|---|---|---|---|---|
| | HR (95% CI) | p-value | HR (95% CI) | p-value |
| Age (per 5-year increase) | 1.03 (1.02 to 1.04) | **<0.0001** | 1.03 (1.02 to 1.05) | **<0.0001** |
| Sex | 1.11 (0.83 to 1.48) | 0.4992 | 1.32 (0.94 to 1.87) | 0.1091 |
| LVEF (per 5% decrease) | 1.12 (1.06 to 1.19) | **0.0001** | 1.11 (1.03 to 1.19) | **0.0059** |
| LVEF ≤40% | 1.93 (1.39 to 2.69) | **0.0001** | 1.56 (1.06 to 2.29) | **0.0239** |
| Chronic kidney disease | 1.91 (1.34 to 2.72) | **0.0004** | 2.98 (2.02 to 4.38) | **<0.0001** |
| Cancer (active) | 1.42 (0.95 to 2.14) | 0.0869 | 1.93 (1.26 to 2.98) | **0.0028** |
| Hypercholesterolemia | 0.61 (0.42 to 0.88) | **0.0084** | 0.62 (0.39 to 0.98) | **0.0423** |
| Diabetes mellitus | 1.50 (1.11 to 2.05) | **0.0093** | — | — |

Abbreviations: CI, confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction; MACE, major cardiovascular cardiac event.

Table adapted from Alrumayh et al. (2025).[16]